

# All-Cause Health Care Utilization and Costs Associated with Newly Diagnosed Multiple Sclerosis in the United States

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## ABSTRACT

**BACKGROUND:** Multiple sclerosis (MS) is a costly and crippling neurologic disease. Approximately 250,000 to 400,000 persons in the United States are currently diagnosed with MS. Most individuals experience their first symptoms between the ages of 20 and 40 years; therefore, this disease may have substantial impact over many years of life on health, quality of life, productivity, and employment. Whereas a number of studies have utilized a cross-sectional design to evaluate the costs associated with MS, no study has used a large administrative claims database to analyze the direct costs associated with newly diagnosed MS.

**OBJECTIVE:** To estimate the additional health care utilization and costs in otherwise healthy patients with newly diagnosed MS.

**METHODS:** This was a retrospective cohort analysis of the Medstat MarketScan Commercial Claims and Encounters database, which is composed of medical and pharmacy claims for approximately 8 million beneficiaries from 45 U.S. commercial health plans. Cases extracted from the database included adults aged 18 to 64 years with either (a) at least 2 medical claims with a diagnosis of MS (ICD-9-CM code 340) in any diagnosis field on the claim or (b) 1 prescription (medical or pharmacy) claim for injectable MS drug therapy (interferon beta-1a, interferon beta-1b, glatiramer acetate) for dates of service between January 1, 2004, and December 31, 2006. Natalizumab was not used to identify MS cases, but was used to exclude potential comparison group subjects. The index date for patients with MS was the first qualifying diagnosis or pharmacy claim. Each MS patient was matched to 5 "healthy comparison" cases without MS diagnoses or treatment using the following variables: region, insurance type, gender, relation to employee, age, and enrollment period. Cases with any condition listed in the Charlson Comorbidity Index were excluded from both the MS and "healthy comparison" cohorts. Each "healthy comparison" case was assigned the index date of the matching MS patient. Continuous enrollment 12 months pre- and post-index was required for both the MS and "healthy comparison" groups. Costs broken down by type of utilization were adjusted to 2010 dollars using the appropriate medical component of the Consumer Price Index. Use of services and costs were compared using chi-square, t-tests, parametric and nonparametric tests.

**RESULTS:** 1,411 MS cases (65.6% female) were matched to 7,055 "healthy comparison" cases (65.6% female). In the analyses of all-cause health care services during the 12-month post-index period, MS patients were significantly more likely to use all categories of health services examined. Compared with the "healthy comparison" group, new MS patients were 3.5 times as likely to be hospitalized (15.2% vs. 4.3% for MS vs. comparison, respectively), twice as likely to have at least 1 emergency room (ER) visit (25.5% vs. 12.2%) and 2.4 times as likely to have at least 1 visit for physical, occupational, or speech therapy (23.7% vs. 9.9%;  $P < 0.001$  for all comparisons). MS patients also had higher mean 12-month costs related to each category of service (inpatient services \$4,110 vs. \$836;

radiology services \$1,693 vs. \$259; ER \$432 vs. \$189; office visits \$849 vs. \$310; therapies \$295 vs. \$81, respectively; all  $P$  values  $< 0.001$ ). Total mean 12-month all-cause health care costs were significantly higher for MS patients than for the "healthy comparison" group (\$18,829 vs. \$4,038, respectively,  $P < 0.001$ ). Claims attributed to MS by diagnosis code in any field on the claim or use of an MS injectable drug accounted for a mean cost of \$8,839 (46.9%), and MS injectable drugs accounted for \$4,573 (24.3%) of total all-cause health care costs.

**CONCLUSIONS:** Newly diagnosed MS patients have significantly higher rates of hospitalizations, radiology services, and ER and outpatient visits compared with non-MS "healthy comparison" patients. MS presents a considerable burden to the U.S. health care system within the first year of diagnosis.

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*This article is the subject of a commentary that appears on pages 713-717 of this issue.*

## What is already known about this subject

- The economic burden associated with multiple sclerosis (MS) is substantial. Patients with MS incur medical costs 2 to 3 times those of all enrollees in a managed care organization.
- The majority of total costs incurred by patients with MS are direct medical costs. In a cross-sectional study of U.S. patients with MS, 94% of whom were using disease-modifying drugs (DMDs), Kobelt et al. (2006) found that 34% of total costs (direct and indirect) were attributable to DMDs.

## What this study adds

- This is the first such study to assess the direct health care costs and resource utilization among newly diagnosed MS patients compared with healthy members of commercial health plans. Overall medical costs were 4.7 times higher for newly diagnosed MS patients.
- Less than one-half of the nearly \$19,000 in the first 12 months of costs after diagnosis of MS could be attributed to medical claims with diagnosis codes for MS in any field on the claim.
- MS injectable drugs accounted for approximately one-fourth of total direct medical costs for newly diagnosed MS patients in the first 12 months after diagnosis.

Multiple sclerosis (MS) is a costly and crippling neurologic disease. Approximately 250,000 to 400,000 persons in the United States are currently diagnosed with MS.<sup>1-3</sup> Most individuals experience their first symptoms between the ages of 20 and 40 years; therefore, this disease may have substantial impact over many years of life on their health, quality of life, productivity and employment.<sup>4</sup> As a consequence, the economic costs associated with MS are significant.<sup>4</sup>

Managing MS requires both pharmacologic and nonpharmacologic treatments to prevent disease progression and control a variety of related disorders. Specific disorders related to the progression of MS may require physical therapy, occupational therapy, medical devices, counseling, or medications. These disorders include fatigue, bladder or bowel dysfunction, urinary tract infections, muscular weakness, spasticity, joint contractures, difficulty walking, tremor, vision disturbances, pain, loss of cognition, depression and anxiety, speech and swallowing difficulty, sexual dysfunction, and pressure ulcers.<sup>5</sup> The objectives of the treatment of MS are to avoid temporary disability attributed to relapses and to delay progression to permanent disability.

Two published studies and 1 poster abstract have used cross-sectional designs to evaluate the costs associated with MS and MS relapses,<sup>6-8</sup> and 2 studies have evaluated direct and indirect costs of the disease through surveys.<sup>9,10</sup> No published studies in the literature used data from a large, nationally representative administrative claims database to evaluate the direct costs (e.g., medical, pharmacy) of newly diagnosed MS patients. One needs to be able to estimate the trade-offs involved in introducing costly treatment to newly diagnosed MS patients.

The purpose of this study was to examine the burden on the U.S. health care system, in service use and cost, associated with newly diagnosed MS by assessing the direct costs and resource utilization (inpatient, outpatient, pharmacy, and emergency room [ER] visits) associated with MS diagnosis or treatment compared with a matched "healthy comparison" group from a U.S. managed care perspective in an adult population aged 65 years or younger.

## Methods

This was a retrospective analysis utilizing a large, nationally representative administrative U.S. claims database, the Medstat MarketScan Commercial Claims and Encounters (CCE) dataset. The CCE dataset contains the health care experience of approximately 8 million employees and their dependents (annually) covered under preferred provider organizations, point-of-service plans, indemnity plans, and health maintenance organizations. In addition, the database provides data on hospitalizations, ER visits, diagnosis, age of patient, gender, geographic location, inpatient and outpatient services, and outpatient prescription drugs. Medstat has separate files for inpatient, outpatient (includes ER, hospital outpatient,

**TABLE 1** Service Types and Drug Codes

Services	Codes Used
<b>Service types<sup>a</sup></b>	
Occupational therapy	Service code 114
Physical therapy	Service code 115
Speech and language therapy	Service code 116
<b>Injections<sup>b</sup></b>	
	MS drugs - any of the following procedure codes: J1830, J1825, Q3025, Q3026, J1595, Q2010, Q4079
Physician office visits	Any of the following CPT codes: 99201-99205, 99211-99215, 99241-99245, 99271-99274, 99381-99387, 99391-99397, 99401-99404, 99420, 99429
Neurologist office visits	Field listed as 260, which is neurologist
Laboratory	CPT code 8xxxx (i.e., 80000-89999)
Radiology	CPT 7xxxx (i.e., 70000-79999)
PT/OT/speech, swallowing therapy)	Service field = 114-116, which is therapy CPT codes 97001-97799, 92506-92508, 92526; HCPCS codes G0152, G0153, S9128, S9129
<b>Drugs</b>	
<b>NDC Numbers (First 9 Characters)</b>	
Glatiramer acetate	00088115003; 00088115330; 68115075030; 68546031730 <sup>c</sup>
Interferon beta-1a	44087002203; 44087004403; 44087882201; 54569443300 <sup>c</sup> ; 59627000103; 59627000205
Interferon beta-1b	50419052103 <sup>c</sup> ; 50419052115; 50419052315; 50419052325; 50419052335 <sup>c</sup>
Natalizumab	59075073015 <sup>b</sup>
<b>J Codes<sup>d</sup></b>	
Glatiramer acetate	J1595; Q2010
Interferon beta-1a	J1825; Q3025
Interferon beta-1b	J1830; Q3026
Natalizumab	Q4079

<sup>a</sup>99% of the therapies were captured using the occupational, physical and speech and language therapies. Also used specific CPT/HCPCS codes which accounted for the remaining 0.1% of the therapies: 97001-97799, 92506, 92507, 92508, G0153, S9128, 92526.

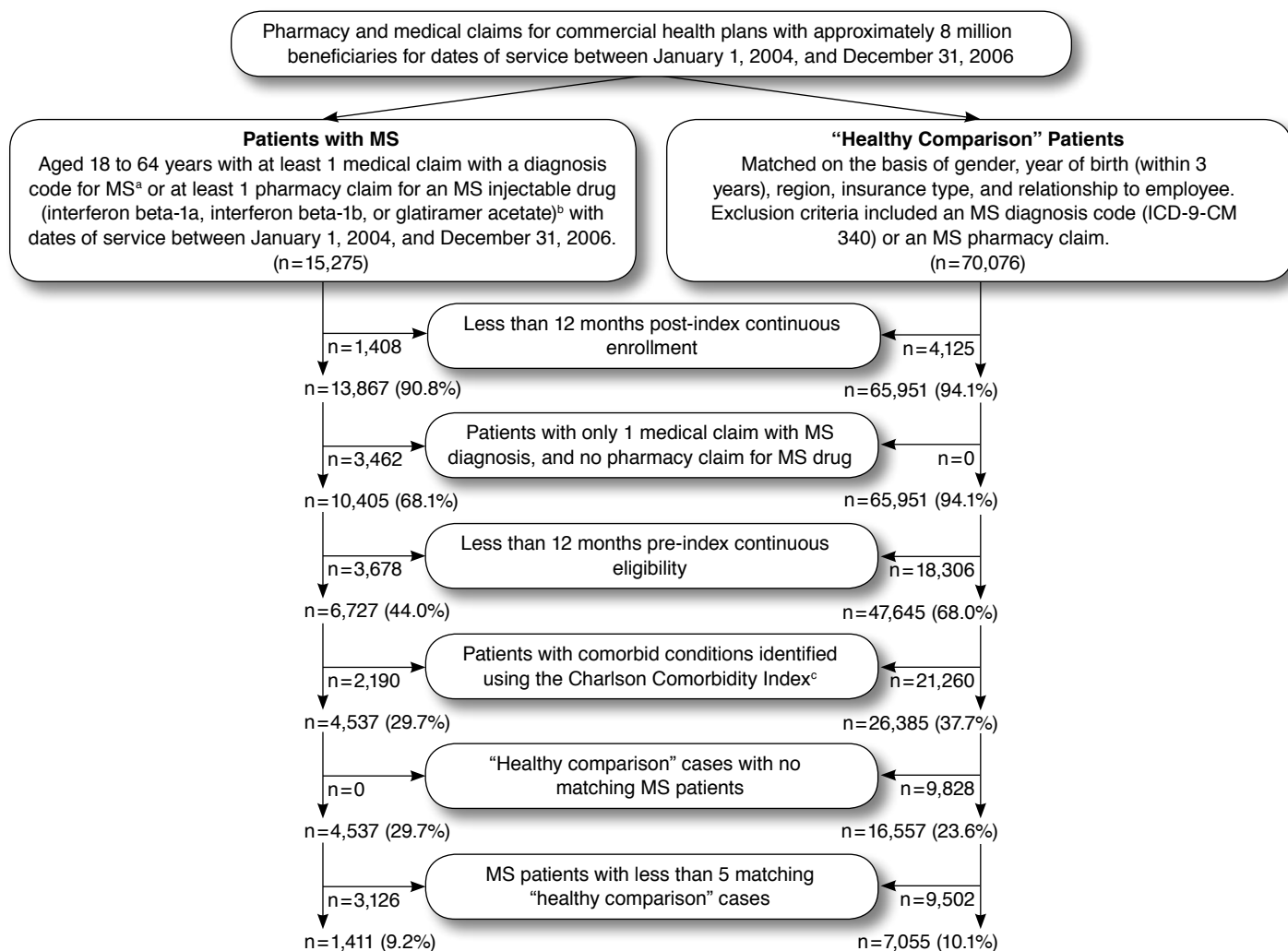
<sup>b</sup>Measured only during the 12-month follow-up, not during sample selection.

<sup>c</sup>No claims were found with this NDC number.

<sup>d</sup>All of these J codes appeared in the database.

CPT = Current Procedural Terminology; HCPCS = Healthcare Common Procedure Coding System; MS = multiple sclerosis; NDC = national drug code; OT = occupational therapy; PT = physical therapy.

and physician visits) and outpatient pharmacy claims. The definitions depicted in Table 1 reflect the manner in which the service categories were assigned whereby the appropriate procedure codes were assigned according to the injections, MS drugs, physician visits, neurologist visits (subset of physician visits), laboratory, physical therapy, occupational therapy, and swallowing therapy. The Medstat database links enrollment and medical claims for inpatient, outpatient, and outpatient prescription drug services for each patient using encrypted identifiers. The data are drawn from roughly 45 large employers, health plans, and government organizations.

**FIGURE 1** Sample Selection Flowchart

<sup>a</sup>Any diagnosis code on the claim was used to define multiple sclerosis (ICD-9-CM code 340) whether it was primary or secondary or thereafter; there were up to 15 diagnosis codes for inpatient claims and 2 diagnosis codes for outpatient claims.

<sup>b</sup>Medical claims for injectable MS medications were not included in the sample selection process.

<sup>c</sup>Identified using any diagnosis field on the claim during the 12 months prior to the index date.

ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification; MS = multiple sclerosis.

Cases extracted from the CCE dataset included adults (aged 18 to 64 years) with (a) a diagnosis code for MS (*International Classification of Diseases, Ninth Revision, Clinical Modification* [ICD-9-CM] = 340) in any claim field (i.e., primary, secondary, or other) on at least 2 claims (inpatient or outpatient medical), or (b) at least 1 outpatient pharmacy claim for MS treatment including interferon-beta 1a (Avonex [Biogen Idec] or Rebif [Pfizer]), interferon-beta 1b (Betaseron [Bayer]), or glatiramer acetate (Copaxone [Teva Pharmaceuticals]) for MS treatment with dates of service between January 1, 2004, and December

31, 2006. Natalizumab (Tysabri [Elan]) was counted as an MS-related drug in the analysis of utilization and cost, and for excluding potential comparison group subjects. However, it was not used for the purpose of identifying MS cases.

The first qualifying MS diagnosis (ICD-9-CM 340, any listed diagnosis) or MS-specific treatment medication was considered to be the index event. Whenever inpatient records were checked for an MS diagnosis, only the admission claim record (up to 15 listed diagnosis codes) was used, and not line-item charges. Thus, an inpatient record with a line item with an

**TABLE 2** Demographic Characteristics

Demographic Characteristics (All Used for Matching)	MS Patient Cohort <sup>a</sup>		Healthy Comparison Cohort <sup>a</sup>		Full Sample	
	n = 1,411		n = 7,055		n = 8,466	
Mean [SD] age	43.2	[12.8]	44.2	[12.8]	44.1	[12.8]
	%	(n)	%	(n)	%	(n)
<b>Sex</b>						
Female	65.6	(926)	65.6	(4,630)	65.6	(5,556)
Male	34.3	(485)	34.4	(2,425)	34.3	(2,910)
<b>Relationship to primary insured</b>						
Self	68.0	(960)	68.0	(4,800)	68.0	(5,760)
Spouse	23.1	(326)	23.1	(1,630)	23.1	(1,956)
Child or other dependent	8.9	(125)	8.9	(625)	8.9	(750)
<b>U.S. Bureau of Census region</b>						
North central	31.3	(441)	31.3	(2,205)	31.3	(2,646)
Northeast	12.0	(170)	12.1	(850)	12.1	(1,020)
South	33.4	(471)	33.4	(2,355)	33.4	(2,826)
West	23.3	(329)	23.3	(1,645)	23.3	(1,974)
<b>Insurance plan type</b>						
Noncapitated point of service	24.7	(349)	24.7	(1,745)	24.7	(2,093)
Preferred provider organization	27.5	(388)	27.5	(1,940)	27.5	(2,328)
Capitated point of service	3.3	(46)	3.3	(230)	3.3	(276)
Health maintenance organization	33.5	(472)	33.5	(2,360)	33.5	(2,832)
Comprehensive <sup>b</sup>	11.1	(156)	11.1	(780)	11.1	(936)
<b>Identification year</b>						
2004	43.2	(609)	43.2	(3,045)	43.2	(3,654)
2005	30.3	(427)	30.3	(2,135)	30.3	(2,562)
2006	26.6	(375)	26.6	(1,875)	26.6	(2,250)
<b>Method of identification</b>						
MS diagnosis only	96.0	(1,354)	Not applicable		Not applicable	
MS medication only	3.8	(54)	Not applicable		Not applicable	
Both MS diagnosis and MS medication <sup>c</sup>	0.2	(3)	Not applicable		Not applicable	

<sup>a</sup>Both cohorts excluded patients with any comorbidities, identified using the Charlson Comorbidity Index, measured using any diagnosis code on the claim during the 12 months prior to the index date.

<sup>b</sup>Comprehensive insurance plan denotes major medical which is synonymous with indemnity plan.

<sup>c</sup>Indicates that patient had both a diagnosis and a claim for MS medication on the same day.

MS = multiple sclerosis; SD = standard deviation.

MS diagnosis code was not considered an MS claim if the MS diagnosis code failed to make it into the header claim's list of up to 15 diagnoses.

Patients were excluded if they were not continuously enrolled for at least 12 months pre-index event and at least 12 months post-index event or if they were missing necessary data elements (e.g., age, gender, location, plan type, or diagnosis codes). Patients were also excluded if they had an MS diagnosis or treatment within 12 months prior to the index date.

Each qualifying MS case was matched to 5 "healthy comparison" group enrollees with the same geographic region of country, insurance type, gender, relation to employee, and age of patient at index event date (year of birth within 3 years). "Healthy comparison" group enrollees could not have an MS diagnosis code or MS treatment drug in the study period. "Healthy comparison" group enrollees also had matching

enrollment—that is, they were enrolled at the time of the index date of the matched MS patient, and were continuously enrolled from 12 months prior to the index date to at least 12 months following the index date. The inclusion of 5 matched "healthy comparison" group enrollees rather than 1:1 matching was to improve power. Both MS patients and "healthy comparison" group enrollees were excluded if they had a history of any condition in the Charlson Comorbidity Index (CCI) during the 12 months prior to the index date.<sup>11</sup> All listed diagnosis codes were used for this purpose. Excluding people with comorbid conditions allowed for analyses that isolate the impact of newly diagnosed MS. It also avoids the difficulty in controlling for severity of comorbidities.

### Statistical Analysis Plan

Utilization rates and costs for prescription drugs and health

**TABLE 3** Prescription Drug Utilization in 12-Month Post-Index Period

Prescription Medication Utilization	MS Patient Cohort <sup>a</sup>		Healthy Comparison Cohort <sup>a</sup>		P Value <sup>b</sup>
	n = 1,411		n = 7,055		
MS drugs <sup>c</sup>					
Patients with any pharmacy claim % (n)	30.8%	(435)	Not applicable		
Mean [SD] number of pharmacy claims	2.30	[4.06]	Not applicable		
Mean [SD] number of pharmacy claims per user	7.46	[3.89]	Not applicable		
Anticonvulsants					
Patients with any pharmacy claims % (n)	21.2%	(299)	3.4%	(240)	<0.001
Mean [SD] pharmacy claims	1.20	[3.56]	0.19	[1.46]	<0.001
Mean [SD] pharmacy claims per user	5.67	[5.87]	5.60	[5.64]	0.620
Antidepressants					
Patients with any pharmacy claims % (n)	33.1%	(467)	14.6%	(1,030)	<0.001
Mean [SD] pharmacy claims	2.08	[4.00]	0.87	[2.79]	<0.001
Mean [SD] pharmacy claims per user	6.28	[4.67]	5.99	[4.77]	0.147
Antipsychotics					
Patients with any pharmacy claims % (n)	2.4%	(34)	0.6%	(39)	<0.001
Mean [SD] pharmacy claims	0.09	[0.73]	0.02	[0.46]	<0.001
Mean [SD] pharmacy claims per user	3.71	[3.00]	4.49	[4.39]	0.996
Urinary antibiotics					
Patients with any pharmacy claims % (n)	3.8%	(54)	2.0%	(141)	<0.001
Mean [SD] pharmacy claims	0.07	[0.50]	0.03	[0.23]	<0.001
Mean [SD] pharmacy claims per user	1.94	[1.74]	1.42	[0.82]	0.050
Amphetamines					
Patients with any pharmacy claims % (n)	7.3%	(103)	1.2%	(85)	<0.001
Mean [SD] pharmacy claims	0.29	[1.43]	0.07	[0.77]	<0.001
Mean [SD] pharmacy claims per user	4.00	[3.63]	5.64	[4.28]	0.002
Adrenals					
Patients with any pharmacy claims % (n)	25.4%	(358)	10.0%	(706)	<0.001
Mean [SD] pharmacy claims	0.55	[1.46]	0.19	[0.85]	<0.001
Mean [SD] pharmacy claims per user	2.15	[2.23]	1.88	[2.01]	<0.001
All other prescription drugs					
Patients with any pharmacy claims % (n)	86.8%	(1,225)	74.3%	(5,241)	<0.001
Mean [SD] pharmacy claims	15.20	[18.29]	9.40	[13.04]	<0.001
Mean [SD] pharmacy claims per user	17.53	[18.57]	12.66	[13.70]	<0.001

<sup>a</sup>Both cohorts excluded patients with any comorbidities, identified using the Charlson Comorbidity Index, measured using any diagnosis code on the claim during the 12 months prior to the index date.

<sup>b</sup>P value for Fisher's exact test for proportions and Wilcoxon rank-sum (also known as Mann-Whitney U) test for continuous variables, comparing the MS patient and healthy comparison cohorts.

<sup>c</sup>Does not include injectable MS medications reported on medical claims. 1.4% of patients in the MS cohort had no pharmacy claims for MS injectable drugs but had at least 1 medical claim for an MS injectable drug.

MS = multiple sclerosis; SD = standard deviation.

care services were compared for the MS patient cohort and "healthy comparison" group. Drug use was categorized for many drug categories commonly used in patients with MS: adrenals, amphetamines, anticonvulsants, antidepressants, antipsychotics, urinary antibiotics. These categories were based on therapeutic drug class according to the *Red Book*, which is included in the Medstat database (Appendix).<sup>12</sup> Prescription drug use and health care service utilization were evaluated in terms of whether certain types of drugs or services were used, and how frequently. Drug cost was assessed as the ingredient cost, which represents the discount below the average whole-

sale price, plus the dispensing fee. Service utilization cost was the gross average payment to the provider, and represents the amount eligible for payment under the medical plan. Mean costs were determined overall and by categories of drug use and service utilization. Costs were adjusted to 2010 utilizing the Consumer Price Index. Services with an MS diagnosis in any diagnosis field on the claim were also described.

For statistical analysis, comparison of categorical variables was done using chi-square tests with Fisher's exact test used for comparison of 2 dichotomous variables. Comparison of continuous variables was handled conservatively, using the



**TABLE 4** Health Care Services Utilization in 12-Month Post-Index Period

	MS Patient Cohort <sup>a</sup>		Healthy Comparison Cohort <sup>a</sup>		P Value <sup>b</sup>
Health Care Service Utilization	n = 1,411		n = 7,055		
<b>Inpatient admissions</b>					
Patients with any admission % (n)	15.2%	(214)	4.3%	(303)	<0.001
Mean [SD] number of admissions	0.22	[0.62]	0.05	[0.26]	<0.001
Mean [SD] number of admissions per user	1.42	[0.90]	1.16	[0.54]	<0.001
<b>ER visits</b>					
Patients with any ER visits % (n)	25.5%	(360)	12.2%	(861)	<0.001
Mean [SD] number of ER visits	0.42	[1.08]	0.18	[0.69]	<0.001
Mean [SD] number of visits per user	1.66	[1.58]	1.43	[1.44]	<0.001
<b>Injections, MS treatment drugs<sup>c</sup></b>					
Patients with any MS injections % (n)	1.8%	(25) <sup>d</sup>	0.0%	(0)	<0.001
Mean [SD] number of MS injections	0.14	[1.37]	Not applicable		<0.001
Mean [SD] number of MS injections per user	8.04	[6.69]	Not applicable		<0.001
<b>Physician visits, all</b>					
Patients with any visit % (n)	95.6%	(1,349)	78.9%	(5,566)	<0.001
Mean [SD] number of physician visits	8.08	[6.69]	3.47	[3.92]	<0.001
Mean [SD] number of physician visits per user	8.45	[6.61]	4.40	[3.93]	<0.001
<b>Neurologist visits</b>					
Patients with any visit % (n)	51.0%	(720)	1.5%	(109)	<0.001
Mean [SD] number of neurologist visits	1.74	[2.35]	0.03	[0.30]	<0.001
Mean [SD] number of neurologist visits per user	3.41	[2.26]	2.99	[1.38]	<0.001
<b>Laboratory</b>					
Patients with any service % (n)	80.8%	(1,140)	61.8%	(4,360)	<0.001
<b>Radiology</b>					
Patients with any service % (n)	78.4%	(1,106)	46.8%	(3,302)	<0.001
<b>PT/OT/speech, swallowing</b>					
Patients with any service % (n)	23.7%	(335)	9.9%	(698)	<0.001
Mean [SD] number of therapy sessions	4.85	[15.45]	1.73	[9.88]	<0.001
Mean [SD] number of therapy sessions per user	20.48	[26.26]	17.47	[26.67]	0.096

<sup>a</sup>Both cohorts excluded patients with any comorbidities, identified using the Charlson Comorbidity Index, measured using any diagnosis code on the claim during the 12 months prior to the index date.

<sup>b</sup>P value for Fisher's exact test for proportions and Wilcoxon rank-sum (also known as Mann-Whitney U) test for continuous variables, comparing the MS patient and healthy comparison cohorts.

<sup>c</sup>Indicates only MS injections identified using HCPCS codes on medical claims.

<sup>d</sup>1.8% had a medical claim with a HCPCS code for an injectable MS treatment drug. For 1.4%, this represented their only use of injectable MS treatment drugs, i.e., they had no pharmacy claims for an MS injectable.

ER=emergency room; HCPCS=Healthcare Common Procedure Coding System; MS=multiple sclerosis; OT=occupational therapy; PT=physical therapy; SD=standard deviation.

nonparametric Wilcoxon rank-sum test to account for non-normality.

## Results

A total of 1,411 MS patients and 7,055 "healthy comparison" group enrollees met all sample selection criteria (Figure 1). In both groups, 65.6% of the study sample was female (Table 2). Mean ages were 43 years for MS patients and 44 years for "healthy comparison" group enrollees; 68.0% of enrollees in each cohort were the primary insured, 23.1% were spouses, and 8.9% were dependents.

In this sample, 30.8% of MS patients filled prescriptions for MS treatment drugs, and another 1.4% did not have a pharmacy claim for an MS treatment drug but did have it

administered in a physician's office or ER (Table 3). Thus, a total of 32.2% received an injectable MS treatment drug during the year of follow-up. These patients had an average of 7.5 pharmacy claims. In all drug categories examined, the MS patient cohort had significantly ( $P<0.001$ ) higher use than the "healthy comparison" cohort. This was particularly noteworthy when comparing use of anticonvulsants (21.2% with MS group vs. 3.4% among "healthy comparison" enrollees,  $P<0.001$ ), antidepressants (33.1% with MS group vs. 14.6% among "healthy comparison" enrollees,  $P<0.001$ ), antipsychotics (2.4% with MS group vs. 0.6% among "healthy comparison" enrollees,  $P<0.001$ ), and amphetamines (7.3% with MS group vs. 1.2% among "healthy comparison" enrollees,  $P<0.001$ ). Among users of anticonvulsants, MS patients had a mean of

**TABLE 5** Mean Health Care Expenditures in 12-Month Post-Index Period

Health Care Expenditures by Service Category	MS Patients <sup>a</sup> n = 1,411 Mean [SD] Dollars	Healthy Comparison <sup>a</sup> Cohort n = 7,055 Mean [SD] Dollars	P Value <sup>b</sup>
Inpatient services	4,110 [19,673]	836 [6,929]	<0.001
MS diagnosis on claim <sup>c</sup>	1,802 [12,846]	—	
Emergency room services	432 [1,290]	189 [850]	<0.001
MS diagnosis on claim <sup>c</sup>	53 [354]	—	
Injections, MS drugs <sup>d</sup>	137 [1,605]	—	
Physician visits, all	849 [879]	310 [526]	<0.001
MS diagnosis on claim <sup>c</sup>	265 [366]	—	
Neurologist visits	615 [4,244]	4 [39]	<0.001
MS diagnosis on claim <sup>c</sup>	153 [297]	—	
Laboratory services	409 [990]	140 [348]	<0.001
MS diagnosis on claim <sup>c</sup>	82 [318]	—	
Radiology services	1,693 [3,801]	259 [1,326]	<0.001
MS diagnosis on claim <sup>c</sup>	705 [1,720]	—	
PT/OT/speech, swallowing	295 [1,019]	81 [487]	<0.001
MS diagnosis on claim <sup>c</sup>	75 [602]	—	
Other outpatient services	4,753 (11,209)	1,404 [5,003]	<0.001
MS diagnosis on claim <sup>c</sup>	1,285 [4,213]	—	
Outpatient pharmacy	6,151 [8,574]	817 [1,700]	<0.001
MS drugs <sup>e</sup>	4,436 [7,828]	—	
Anticonvulsants	165 [701]	29 [309]	<0.001
Antidepressants	194 [479]	82 [314]	<0.001
Antipsychotics	24 [253]	6 [132]	<0.001
Urinary antibiotics	3 [23]	1 [7]	<0.001
Amphetamines	81 [444]	8 [111]	<0.001
Adrenals	24 [144]	12 [107]	<0.001
Other	1,225 [3,070]	679 [1,492]	<0.001
<b>Total</b>	<b>18,829 [28,973]</b>	<b>4,038 [10,588]</b>	<b>&lt;0.001</b>
Claims with MS diagnosis or treatment <sup>f</sup>	8,839 [17,825]	0	

<sup>a</sup>Both cohorts excluded patients with any comorbidities, identified using the Charlson Comorbidity Index, measured using any diagnosis code on the claim during the 12 months prior to the index date.

<sup>b</sup>P value for Wilcoxon rank-sum (also known as Mann-Whitney U) test, comparing the MS patient and healthy comparison cohorts.

<sup>c</sup>Indicates a claim with an MS diagnosis in any field—up to 15 fields on an inpatient claim and up to 2 fields on an outpatient claim.

<sup>d</sup>Indicates an MS drug reported using a HCPCS code on a medical claim.

<sup>e</sup>Indicates a pharmacy claim with an NDC number for an MS drug.

<sup>f</sup>Sum of (a) medical claims with MS diagnosis plus (b) medical claims for MS injections plus (c) pharmacy claims for MS drugs.

HCPCS=Healthcare Common Procedure Coding System; MS= multiple sclerosis; NDC=national drug code; OT=occupational therapy; PT=physical therapy; SD=standard deviation.

5.7 pharmacy claims. For antidepressants, the mean was 6.3, for antipsychotics it was 3.7, and for amphetamines it was 4.0. Among MS patients, 25.4% filled a prescription for an adrenal medication compared with 10.0% ( $P<0.001$ ) for the “healthy comparison” enrollees. This category includes prednisone, commonly used in treating acute symptoms of MS.

MS patients were 3.5 times as likely as their “healthy comparison” counterparts to be hospitalized (15.2% vs. 4.3%,  $P<0.001$ ), 2.1 times as likely to have an ER visit (25.5% vs. 12.2%,  $P<0.001$ ), and more likely to have physician office visits (95.6% vs. 78.9%,  $P<0.001$ ), neurologist visits (51.0% vs. 1.5%,  $P<0.001$ ), laboratory tests (80.8% vs. 61.8%,  $P<0.001$ ), radiology services (78.4% vs. 46.8%,  $P<0.001$ ) and physical

therapy (23.7% vs. 9.9%,  $P<0.001$ ; Table 4). MS patients averaged more than 8 physician office visits, and of those seeing a neurologist, the mean number of neurologist visits was 3.4. Only 1.8% of MS patients received injections for MS treatment in an outpatient (or ER) setting; they had a mean of 8.0 such injections during the year. MS patients who received physical therapy had a mean of 20.5 therapy sessions.

The total all-cause health care costs for MS patients over a 12 month post-index period were 4.7 times the costs for “healthy comparison” patients (\$18,829 vs. \$4,038,  $P<0.001$ ) and were significantly higher in every category of utilization (Table 5). MS patients had 7.5 times the pharmacy costs (\$6,151 vs. \$817,  $P<0.001$ ), nearly 5 times the inpatient cost

(\$4,110 vs. \$836,  $P < 0.001$ ), and 6.5 times the radiology cost (\$1,693 vs. \$259,  $P < 0.001$ ).

The mean pharmacy cost for MS treatment drugs was \$4,436, 72% of the total pharmacy cost. Of the \$4,110 mean inpatient cost for MS patients, only \$1,802 had an MS diagnosis on the claim. Similar patterns were found for other service utilization. Overall, the mean cost associated with MS treatment drugs or claims with an MS diagnosis was \$8,839, representing less than one-half (46.9%) of the overall total costs. The remaining \$9,990 (53.1% of the total costs), seemingly unrelated to MS, still represented 2.5 times the total mean cost for the comparison group enrollees ( $P < 0.001$ ).

## ■ Discussion

To the best of our knowledge, this is the first such study to assess the direct health care costs and utilization among newly diagnosed MS patients. To report on the direct health care costs and utilization in newly diagnosed patients with MS, we undertook a retrospective analysis of medical and pharmacy claims data among a cohort of newly diagnosed MS patients matched against a “healthy comparison” group. The results of this study provide evidence of the significant burden of early MS on the health care system. The total costs for newly diagnosed MS patients were found to be 4.7-fold (\$18,829 vs. \$4,038,  $P < 0.001$ ) that of “healthy comparison” enrollees during a 12 month post-index period. Like many other chronic, systemic illnesses, there was a large additional cost of services beyond MS treatment that could not be related to MS by a diagnosis code.

Prescott et al. (2007) examined costs for all MS patients in 2004 with at least 1 diagnosis for MS or at least 1 prescription for an MS treatment drug using a large U.S. claims database but did not evaluate newly diagnosed MS patients exclusively.<sup>13</sup> They found that the mean annual direct MS-related medical cost was approximately \$13,000 (in 2004 dollars). This was much higher than our mean of \$8,839. However, Prescott et al. aggregated costs by Episode Treatment Grouper software, a much more liberal definition of MS-related than used in this study where each specific claim had to include an MS diagnosis code. They also included all patients with MS activity as opposed to this study of apparent newly diagnosed cases, and required only 1 diagnosis of MS without prescription of MS drug as opposed to this study which required 2 diagnosis codes in the absence of an MS treatment drug prescription. Prescott et al. reported that 58% filled a prescription for an MS treatment drug, compared with 31% in the present study. The Prescott et al. study also found that 61% of the MS-related cost of care was attributable to the cost of MS injectable pharmacy claims, as compared with one-half (\$4,436 of \$8,839) in the present study. This discrepancy might be explained by the difference in samples.

Pope et al. (2002) determined the direct all-cause medical costs of MS patients in insured populations.<sup>14</sup> Study data were administrative claims from commercial insurers for 1994 and 1995, Medicare for 1996 and 1997, and Medicaid disabled populations for 1991 through to 1996 from 6 U.S. states. They found that the annual insured expenditures were \$7,677 per commercially insured enrollee with MS versus \$2,394 for all commercially insured enrollees. They concluded that insured enrollees with MS are 2 to 3 times more expensive than average insured enrollees. We found that the total all-cause health care costs for patients with MS were nearly 5 times those of healthy comparison enrollees. One explanation for the larger disparity in our study is that we excluded enrollees with major comorbid illness from the sample. This, in turn, would certainly impact the comparability of our study with that of Pope et al. The Pope et al. study compared MS patients to overall averages for the insured population, which includes high-cost patients with other health conditions.

O'Brien et al. (2003) estimated the cost of managing an episode of relapse in MS in the United States in terms of the utilization of inpatient resource use and costs derived from 5 states.<sup>15</sup> They found that the average cost per person for high management level episode was \$12,870 and that hospital care comprised 71% of the costs. O'Brien et al also found that the typical cost per moderate episode was \$1,847 and a mild episode amounted to \$243. Although we did not assess the cost of MS relapses specifically, such relapses may be the driver for the cost differences in hospitalizations between early MS patients and “healthy comparison” patients.

One strength of the present study is that we used a large U.S. administrative claims database (commercial). The group studied was geographically diverse and has included participants with a variety of insurance coverage. We used a full year of history to check for prior MS diagnosis or treatment. This full year of historical claims also creates a good picture of comorbidities. Many studies look at shorter periods of history, which increases sample size at the cost of integrity of the study population. Our use of matching criteria controlled for several demographic factors and comorbidities that are included in the CCI. Our study also benefits from a large sample size of 1,411 MS patients with 5 comparison group cases per patient. The disease definitions for MS were conservative in the sense that 2 claims with MS diagnoses were required for MS (or 1 prescription for an MS treatment drug). Other studies have used only 1 claim.<sup>16</sup> Lastly, by studying newly diagnosed MS patients, we focused on a group that has been neglected in the literature in terms of utilization and cost.

Approximately 32% of MS patients in our study used an MS disease-modifying agent (DMA) in this study, with most of these filling a prescription for a DMA (30.8%) and an additional 1.4% who received a DMA at an outpatient or ER visit yet filled



no prescriptions for a DMA. This is considerably lower than found in other studies<sup>17</sup> such as the North American Research Committee on Multiple Sclerosis (NARCOMS) registry where, in 2001, 45%-50% of relapsing patients were using a DMA.<sup>18</sup> By 2004, use in the NARCOMS registry increased to approximately 55%-65%.<sup>19</sup> Prescott et al. found that 58% of patients with MS activity filled at least 1 prescription for a DMA in 2004. However, a study by Ozminkowski et al. (2004) utilizing the Medstat dataset reported that only 41.2% of patients were treated with a DMA in the year 2000.<sup>16</sup> Furthermore, it is important to note that none of these studies evaluated newly diagnosed MS patients.

### Limitations

The foremost limitation is the exclusion of enrollees with comorbidities, which keeps the focus on the impact of the newly diagnosed MS, but does not reflect the overall group of newly diagnosed MS cases. Second, data from administrative claims databases have intrinsic potential sources of bias. Information that would affect study outcomes such as explicit measures of clinical and disease severity or socioeconomic status are not readily available. Also, the pharmacy utilization data do not include use of over-the-counter (OTC) medications, and expenditures will not include use of complementary or alternative therapies such as chiropractic or acupuncture. However, in the context of the large health care expenses of MS patients, OTC medications and complementary or alternative therapies are unlikely to substantially alter the cost picture. Third, chart review or independent confirmation of coding was not possible. Fourth, the study population was drawn from a sample of individuals and their dependents with employer-sponsored health insurance. As such, the findings from this study may not be generalizable to the entire U.S. population, particularly individuals who are covered under Medicare or Medicaid. Fifth, this study examines patients who have been recently diagnosed with no comorbidities and will not reflect the utilization patterns and costs of patients with long-term or established disease, or with comorbid conditions. Sixth, using 1 year of historical claims data to identify people with no prior diagnosis of MS will inevitably include some patients who were diagnosed more than 12 months prior but had no MS care in the preceding 12 months. Seventh, although 53.1% of the higher utilization and costs for MS patients compared with healthy enrollees could not be directly attributed to an MS diagnosis, it is clear that patients with MS incur higher costs than enrollees without, when both groups are pre-screened to remove patients with comorbidities. MS patients were help-seeking and required to have both insurance coverage and at least 2 encounters with the health care system that were related to their condition, or 1 prescription for an injectable MS treatment drug. Eighth, excluding comorbidity is possible only

to the extent that comorbid diagnoses are coded on medical claims. Ninth, we analyzed claims data from the 3-year period 2004 through 2006, and pharmacy-medical benefits have changed over time.

### Conclusions

Newly diagnosed MS patients have significantly higher rates of hospitalizations, radiology services, and ER and outpatient visits compared with non-MS "healthy comparison" patients. MS presents a considerable burden to the U.S. health care system within the first year of diagnosis.

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### DISCLOSURES

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## APPENDIX Drug Categories and Drugs

Drug Category	Therapeutic Drug Class	Generic Drug Name
Adrenals	166	Beclomethasone, Betamethasone, Budesonide, Cortisone, Desoxycorticosterone, Dexamethasone, Fludrocortisone, Flunisolide, Fluticasone (and combinations), Hydrocortisone, Methylprednisolone, Mometasone Furoate, Prednisolone, Prednisone, Triamcinolone
Amphetamines	71	Amphetamine, Benzphetamine, Dexmethylphenidate, Dextroamphetamine, Diethylpropion, Lisdexamfetamine, Methamphetamine, Methylphenidate, Modafinil, Phendimetrazine, Phentermine
Anticonvulsants	64-68	Carbamazepine, Clonazepam, Divalproex, Ethosuximide, Felbamate, Gabapentin, Lamotrigine, Levetiracetam, Magnesium, Methsuximide, Oxcarbazepine, Phenytoin, Primidone, Tiagabine, Topiramate, Valproic Acid, Zonisamide
Antidepressants	69	Amitriptyline (and combinations), Amoxapine, Bupropion, Citalopram, Clomipramine, Desipramine, Doxepin, Duloxetine, Escitalopram, Fluoxetine, Fluvoxamine, Imipramine, Maprotiline, Mirtazapine, Nefazodone, Nortriptyline, Paroxetine, Phenelzine, Protriptyline, Sertraline, Tranylcypromine, Trazodone, Trimipramine, Venlafaxine
Antipsychotics	70	Aripiprazole, Chlorpromazine, Clozapine, Fluphenazine, Haloperidol, Loxapine, Olanzapine, Paliperidone, Perphenazine, Pimozide, Quetiapine, Risperidone, Thioridazine, Thiothixene, Trifluoperazine, Ziprasidone
Urinary antibiotics	19	Belladonna, Fosfomycin, Methenamine (and combinations), Nitrofurantoin